REMARKS/ARGUMENTS

I. Status of the Claims

Applicants thank the examiner for her time in a telephone interview to discuss the response to the pending office action.

Claims 1, 2, 4-9, and 11-15 will be pending after entry of this amendment. Claims 1 and 11-14 have been amended. Claims 16-18 and 21-29 have been canceled. Support for amendment to the claims can be found throughout the specification and, for example, on page 21, l. 29 to page 22, l. 33, and in Table 1, pages 83-84. Claim amendments are for purposes of improved clarity or consistency of claim language unless otherwise noted. No claim amendment should be construed as an acquiescence in any ground of rejection. No new matter has been added by this amendment.

The amendment is necessary and was not earlier presented because it is in response to the new ground of rejection for new matter set forth in the final Office Action. Since the amendment obviates the outstanding grounds of rejection as discussed below, reduces the number of issues, contains no new matter, and places the application in condition for allowance or better condition for appeal, the amendment should be entered.

Claims 15-18 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 1, 2, 4-9, and 11-15 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Hmama et al. (*Journal of Experimental Medicine*, **190**: 1583-1594, 1999) in view of Baracchini et al. (U.S. Patent 5,801,154) and Fritz et al. (*Journal of Colloid and Interface Science*, **195**: 272-288, 1997). Claims 21-29 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Hmama et al. (*Journal of Experimental Medicine*, **190**: 1583-1594, 1999) in view of Cowsert, L. (U.S. Patent 6,566,133).

II. Information Disclosure Statement

The Information Disclosure Statement, filed September 12, 2003 has been acknowledged by the examiner.

III. Patentability under 35 U.S.C. § 112, first paragraph

Claims 15-18 have been rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Applicants have canceled claims 16-18 without prejudice to pursuing the claims in a continuing application. Applicants traverse the rejection.

To be enabling, "the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." The amount of required experimentation must be reasonable. Enablement may be provided by "illustrative examples," *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993), and the initial burden is on the PTO to demonstrate an objective factual basis for questioning Applicants' disclosure. *Id.* However, the inquiry cannot stray from the metes and bounds of the claim language itself. The invention that must be enabled is that defined by the claims. *Ex parte Erlich*, 3 U.S.P.Q.2d 1011 (Pat. Off. Bd. App. 1987).

While some experimentation may be permitted, "the amount of required experimentation must be reasonable." *White Consolidated Industries*, 713 F.2d 788, 791 (Fed. Cir. 1983) Applicants do not claim a particular level of activity. Rather, their claims are directed to methods for simply modulating gene expression. The specification teaches that the claimed oligonucleotides of the present invention can be used in a method of inhibiting the expression of vitamin D nuclear receptor in cells or tissues comprising contacting the cells or tissues with the oligonucleotide of claim 1 so that expression of vitamin D nuclear receptor is inhibited. Nothing in the Office Action indicates that the claimed compounds will not modulate gene expression to at least some extent. For example, antisense oligonucleotides to human vitamin D nuclear receptors have been used in model systems for treatment of cancer, for example, in investigations of the roles of $1,25(OH)_2D_3$ in osteosarcoma cells, U937 monoblastoid cells, MCF-7 breast cancer cells and ALVA-31 prostatic carcinoma cells. See for example, page 3, l. 33-36 of the specification. The specification provides an enabling disclosure for a method of inhibiting the expression of vitamin D nuclear receptor in cells or tissues.

In view of the foregoing, Applicants submit that claim 15 is fully enabled, and request withdrawal of the rejection under 35 U.S.C. § 112.

IV. Patentability under 35 U.S.C. § 103(a)

Claims 1, 2, 4-9, and 11-15 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hmama et al. (*Journal of Experimental Medicine*, **190**: 1583-1594, 1999) in view of Baracchini et al. (U.S. Patent 5,801,154) and Fritz et al. (*Journal of Colloid and Interface Science*, **195**: 272-288, 1997). Applicants traverse the rejection.

Applicants' claims, as amended, are to an oligonucleotide 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3), wherein the oligonucleotide specifically hybridizes with an 8 to 50 nucleotide region of the nucleic acid molecule encoding human vitamin D nuclear receptor within nucleotides 1599 to 1637 or within nucleotides 1710 to 1757 of SEQ ID NO:3, and inhibits the expression of human vitamin D nuclear receptor. The Examiner states that the Hmama et al. reference discloses a 21-base pair phosphorothioate antisense oligonucleotide targeting the start codon of the human vitamin D nuclear receptor. The Baracchini et al. reference allegedly discloses modified or substituted oligonucleotides. The Fritz et al. reference allegedly discloses a composition comprising an antisense oligonucleotide and a pharmaceutically acceptable carrier or diluent comprising a colloidal dispersion system. The Hmama et al. reference in view of the Baracchini et al. and Fritz et al. references do not teach or disclose oligonucleotide molecules 8 to 50 nucleobases in length, targeted to a nucleic acid molecule encoding human vitamin D nuclear receptor, wherein the oligonucleotide specifically hybridizes with an 8 to 50 nucleotide region of the nucleic acid molecule encoding human vitamin D nuclear receptor within nucleotides 1599 to 1637 or within nucleotides 1710 to 1757 of SEQ ID NO:3, and inhibits the expression of human vitamin D nuclear receptor. The cited references further do not teach the claimed chimeric oligonucleotide. The claimed target region is not taught by the Hmama et al. reference which targets an antisense oligonucleotide to the start codon. Furthermore, modified or substituted oligonucleotides and pharmaceutical compositions comprising antisense oligonucleotides targeted to nucleotides 1599 to 1637 or to nucleotides 1710 to 1757 of SEQ ID NO:3 of a nucleic acid molecule encoding human vitamin D nuclear receptor are patentable over the Hmama et al. reference in view of the Baracchini et al. and the Fritz et al. references. Therefore, claims 1, 2, 4-9, and 11-15 are patentable over the Hmama et al. reference in view of the Baracchini et al. and the Fritz et al. references.

The rejection of claims 1, 2, 4-9, and 11-15 under 35 U.S.C. § 103(a) has been overcome. Therefore, Applicants respectfully request that the rejection be withdrawn.

Claims 21-29 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Hmama et al. (*Journal of Experimental Medicine*, **190**: 1583-1594, 1999) in view of Cowsert, L. (U.S. Patent 6,566,133).

Applicants have canceled claims 21-29 without prejudice to pursuing the claims in a continuing application. Therefore, the rejection of claims 21-29 under 35 U.S.C. § 103(a) is moot.

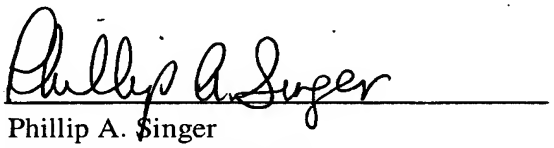
Since the claims patentably define over the prior art, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103(a) be withdrawn.

V. Conclusion

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

Date: March 16, 2003



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